THE EFFECT OF GROUP COGNITIVE BEHAVIOR HYPNOTHERAPY (GCBH) ON NEUROENDOCRINE AND SOMATIC SYMPTOMS IN PATIENTS WITH ANXIETY DISORDERS IN NANJING, CHINA

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by

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LIST OF ABBREVIATIONS

COR	Cortisol
ACTH	Adrenocorticotropic Hormone
T3	Triiodothyronine
T4	Triiodothyronine
TSH	Triiodothyronine
HAMA	Hamilton Anxiety Scale
SSS	Somatic Symptom Self-Rating Scale
SAS	Self-Rating Anxiety Scale
USM	Universiti Sains Malaysia
ISRCTN	International Standard Randomized Controlled Trial Number
CCMD	Chinese Criteria for Classification and Diagnosis of Mental Disorders

LIST OF APPENDICES

KESAN TERAPI TINGKAH LAKU KOGNITIF HIPNOSIS BERKUMPULAN TERHADAP GEJALA NEUROENDOKRIN DAN SOMATIK PADA PESAKIT DENGAN KECELARUAN KEBIMBANGAN DI NANJING, CHINA

ABSTRAK

Prevalens gangguan kecemasan semakin meningkat dan mempunyai kesan yang ketara terhadap kualiti hidup. Kajian ini bertujuan untuk menentukan kesan terapi tingkah laku kognitif hipnosis berkumpulan terhadap gejala somatik dan tahap neuroendokrin pada pesakit dengan kecelaruan kebimbangan. Kajian ini menggunakan reka bentuk percubaan terkawal secara rawak. Sejumlah 84 pesakit yang memenuhi kriteria inklusi dipilih secara rawak dan dibahagikan sama ada kepada kumpulan intervensi (42 peserta) atau kumpulan kawalan (42 peserta) menggunakan pengacakan komputer. Selepas melengkapkan skala pengukuran psikologi (Skala Kecemasan Hamilton (HAMA), Skala Kecemasan Kendiri (SAS), dan Senarai Semak Gejala Somatisasi (SSS)) dan ujian darah (Kortisol (COR), Serum triiodotironin (T3), Tiroksin (T4), Hormon Perangsang Tiroid (TSH) dan Hormon Adrenokortikotropik (ACTH)), kumpulan intervensi menerima terapi tingkah laku kognitif hipnosis berkumpulan sekali seminggu selama enam minggu berturut-turut. Kumpulan kawalan hanya menerima rawatan dan penjagaan rutin. Selepas enam minggu, kedua-dua kumpulan melengkapkan semula skala pengukuran psikologi (HAMA, SAS, SSS) dan ujian darah (COR, ACTH, TSH, T3, T4). Data dianalisis menggunakan ujian chi-square dan ujian t untuk membandingkan perbezaan antara kedua-dua kumpulan. Keputusan menunjukkan bahawa selepas terapi tingkah laku kognitif hipnosis berkumpulan, skor HAMA dalam kumpulan

eksperimen menurun dari 24.79±5.479 kepada 7.52±3.194 (P<0.01), SAS menurun dari 59.07±3.047 kepada 28.14±3.00, dan SSS menurun dari 56.12±3.262 kepada 27.50±1.824 (P<0.001). Keputusan ujian darah untuk COR (581.66±78.241 berbanding 343.05±50.378 nmol/L), ACTH (14.37±1.481 berbanding 12.66±0.775 pmol/L), TSH (3.53±0.657 berbanding 2.83±0.758 mIU/L), T3 (1.22±0.081 berbanding 0.93±0.041 ng/ml), dan T4 (8.32±0.711 berbanding 6.73±0.638 ng/ml) semuanya lebih rendah daripada sebelum rawatan, dengan signifikansi statistik (P<0.001). Pada masa yang sama, kumpulan kawalan menunjukkan penurunan yang ketara dalam skor penuh HAMA (26.88±4.763 berbanding 19.21±2.464) dan SAS (59.07±3.047 berbanding 28.14±3.000) berbanding dengan 6 minggu sebelumnya. (P < 0.001). Kajian ini mendapati bahawa terapi tingkah laku kognitif hipnosis berkumpulan boleh mengurangkan gejala fizikal pada pesakit dengan gangguan kecemasan dan memperbaiki tahap neuroendokrin mereka.

Kata kunci: kecelaruan kebimbangan, simptoms fizikal, neuroendokrin biomarker, terapi tingkah laku kognitif, kajian eksperimen

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ABSTRACT

The prevalence of anxiety disorder is increasing and has a significant impact on quality of life. This study aims to determine the effects of group cognitive behavior hypnotherapy on somatic symptoms and neuroendocrine levels in patients with anxiety disorder. This study utilized a randomized control trial design. A total of 84 patients who met the inclusion criteria were randomly selected and assigned to either the intervention group (42 participants) or the control group (42 participants) using computer randomization. After completing psychological measurement scales (Hamilton Anxiety Scale (HAMA), Self-Rating Anxiety Scale (SAS), and Somatic Symptom Self-Rating Scale (SSS)) and blood tests (Cortisol (COR), Serum triiodothyronine (T3), Thyroxine (T4), Thyroid-Stimulating Hormone (TSH) and Adrenocorticotropic Hormone (ACTH)), the intervention group received group cognitive behavior hypnotherapy once a week for six consecutive weeks. The control group only received routine treatment and care. After six weeks, both groups completed the psychological measurement scales (HAMA, SAS, SSS) and blood tests (COR, ACTH, TSH, T3, T4) again. Data was analyzed using a chi-square test and t-test to compare differences between the two groups. The results showed that after group cognitive behavior hypnotherapy, the HAMA score in the experimental group decreased from 24.79±5.479 to 7.52±3.194 ($P<0.01$), SAS decreased from 59.07±3.047 to 28.14±3.00 , and SSS decreased from 56.12±3.262 to 27.50±1.824

(P<0.001) . The blood test results for COR (581.66±78.241 vs 343.05±50.378 nmol/L), ACTH (14.37±1.481 vs 12.66±0.775 pmol/L), TSH (3.53±0.657 vs 2.83±0.758 mIU/L), T3 (1.22±0.081 vs 0.93±0.041 ng/ml), and T4 (8.32±0.711 vs 6.73±0.638 ng/ml) were all lower than before treatment, with statistical significance (P<0.001). At the same time, the control group showed significant decreases in HAMA (26.88±4.763 VS 19.21±2.464) and SAS(59.07±3.047 VS 28.14±3.000) full scores compared with 6 weeks earlier (P < 0.001). This study found that group cognitive behavior hypnotherapy can alleviate physical symptoms in patients with anxiety disorders and improve their neuroendocrine levels.

Key Words: anxiety disorder, physical symptoms, neuroendocrine biomarker, cognitive-behavioral hypnotherapy, experimental study

CHAPTER 1

INTRODUCTION

1.1 Introduction

This study combines cognitive behavior therapy and hypnotherapy in a group format to improve patients' anxiety symptoms and neuroendocrine levels. This section discusses the detailed background of the study and introduces the epidemiological background of anxiety disorders. The study includes an evaluation of cognitive behavioral therapy, hypnotherapy, and two aspects of anxiety disorder: somatic symptoms and neuroendocrine levels. The latter part of this chapter includes the problem statement and research foundation. Finally, this chapter concludes with the research questions, research objectives, and hypotheses of this study.

1.2 Background of Study

Peoples lives are uncontrollable and constantly accelerating, and competition is becoming increasingly fierce. The degree of personal emotional imbalance is more evident, which has led to a rising trend in the incidence of anxiety disorders (Sijie, 2019). Bareeqa et al. (2021) found that the prevalence of anxiety disorders in China increased to 21.8%, with 48.1% of individuals experiencing stress due to Corona Virus Disease 2019 (COVID-19). Comparison of studies from different Asian countries indicates that the prevalence of anxiety disorder in China is higher than that in India and Singapore (Chew et al., 2020). Anxiety disorders can exist as independent illnesses and are widely present among patients with various physical diseases, and they become complications of these illnesses (Dailin et al., 2017b). In the past, most patients with anxiety disorder were only treated with a single

medication, but the effects were unsatisfactory (Sen et al., 2016); moreover, various adverse reactions, such as attention deficit, drowsiness, drug dependence, and reactions, occurred after discontinuation. This phenomenon affects compliance to some extent. Currently, a combination of medication therapy and psychological therapy is often used in clinical practice.

Many psychological therapy methods are available worldwide. Cognitive behavior therapy (CBT) is the most commonly used psychological therapy method in clinical practice. However, psychodynamic psychologists believe that patients with anxiety and depression have compliance issues because of lack of motivation, avoidance, and negative automatic thinking, resulting in poor therapeutic effects on anxiety symptoms caused by subconscious or deep issues (Fengling et al., 2017). CBT also has certain limitations (John Wiley & Sons, 2004).

Hypnosis has long been overlooked but proven to be excellent in achieving long-lasting relaxation, anxiety, and depression relief as well as pain alleviation (Kohen, 2011). Incorporating hypnosis can reduce patients' psychological defenses, elucidate their state of physical and mental relaxation, increase psychological plasticity, and accept cognitive therapy. This strategy allows for profound behavior correction, helps cultivate new behavioral patterns, and establishes stable and appropriate coping mechanisms (Ramondo et al., 2021).

Cognitive hypnotherapy (CH), shares some similarities with CBT and hypnosis, so these approaches naturally combine (Golden 1983; Heap, 2012). Imagination and relaxation are familiar concepts in hypnosis and CBT. The integration of hypnotherapy and CBT can be traced back to Wolpe who initially used

hypnosis as a part of systematic desensitization to reduce anxiety in patients when facing fear-provoking situations (Wolpe & Turkat, 1985). Cognitive, behavioral, and hypnosis techniques provide foundation for CH. The optimal treatment model of combining hypnosis with CBT will guide patients in mastering self-hypnosis methods and assist them in relaxation outside of therapy sessions to stabilize treatment outcomes (Han Rong et al., 2019)

1.3 Problem Statement

Anxiety disorders represent a prevalent challenge within the realm of mental health, impacting a substantial portion of the global populace. Individuals afflicted by these disorders not only endure enduring emotional turmoil but also grapple with persistent physical manifestations that prove difficult to manage and often unresponsive to conventional treatments. These symptoms tend to persist and recur over time, significantly hindering patients' daily functionality, work efficiency, and overall quality of life. Furthermore, the repercussions extend beyond the individual to strain familial relationships and heighten susceptibility to external pressures within the family dynamic. The emotional responses and behavioral control of family members often deteriorate as they navigate the ongoing anxiety symptoms of their afflicted loved ones, resulting in an overall decline in family cohesion (Xiangli, 2017).

Despite the widespread prevalence of anxiety disorders, current therapeutic modalities encounter substantial challenges in effectively addressing the psychological and physiological symptoms associated with these conditions. While pharmacological interventions can offer relief in certain instances, they frequently

lead to dependence, and adverse effects, and fail to target the underlying cognitive and emotional triggers of anxiety. Psychotherapeutic approaches, such as Cognitive-Behavioral Therapy (CBT), predominantly focus on cognitive distortions and maladaptive behaviors, potentially falling short of alleviating the somatic symptoms and neuroendocrine imbalances commonly present in anxiety disorders. Moreover, existing treatments often lack an integrative approach, concentrating on mental or physical aspects without encompassing a comprehensive strategy that simultaneously addresses both domains.

The present study aims to address these limitations by testing a standardized intervention combining cognitive and hypnosis techniques, known as Group Cognitive-Behavioral Hypnotherapy (GCBH). This study will explore the effectiveness of GCBH in reducing the severity of physical symptoms and normalizing neuroendocrine levels in patients with anxiety disorders. By providing scientific evidence for the efficacy of GCBH, this research seeks to enhance the treatment of anxiety disorders, contributing to the holistic rehabilitation of affected individuals.

1.4 Research Questions

This study aims to answer the following research questions.

1. What are the neuroendocrine levels of patients with anxiety disorders in Nanjing China?

2. How is the severity of physical symptoms among patients with anxiety disorders in Nanjing China?

3. What is the effect of group cognitive behavior hypnotherapy on the severity of physical symptoms in patients with anxiety disorders in Nanjing China?

4. What is the effect of group cognitive behavior hypnotherapy on neuroendocrine level in patients with anxiety disorders in Nanjing China?

1.5 Research Objectives

1.5.1 General objectives

This work aims to determine the effectiveness of group cognitive behavior hypnotherapy (GCBH) on neuroendocrine level and somatic symptoms among patients with anxiety disorders in Nanjing, China.

1.5.2 Specific Objectives

1. To determine the severity of somatic symptoms among patients with anxiety disorders in Nanjing China.

2. To determine the level of neuroendocrine among patients with anxiety disorders in Nanjing China.

3. To determine the effect of group cognitive behavior hypnotherapy on the severity of somatic symptoms among patients with anxiety disorders in Nanjing China.

4. To determine the effect of group cognitive behavior hypnotherapy on neuroendocrine level in patients with anxiety disorders in Nanjing China.

1.6 Research Hypothesis

Two hypotheses were tested in this study:

1. Hypothesis 1: H_o = The severity of somatic symptoms are not significantly different between the intervention group and the control group

H_a = The severity of somatic symptoms are significantly different between the experimental group and the control group.

2. Hypothesis 2: H_o = Neuroendocrine levels are not significantly different between the intervention group and the control group.

H_a = Neuroendocrine levels are significantly different between the intervention group and the control group.

1.7 Definition of terms

Standard and operational definitions used in this study are as follows:

1. Group Cognitive Behavior Hypnotherapy: The combination of CBT and hypnosis treatment that focuses on individuals' thoughts and behaviors in specific situations as well as on how to enhance treatment effectiveness and overcome emotional and behavioral issues.

2. Hypnosis therapy: Through verbal and behavioral cues, patients can be induced to enter a trance state, which narrows the scope of the patient's consciousness and allows the patient to dissociate from the troubling problem, thereby relieving the patient's emotions, changing the patient's thinking, and producing a therapeutic effect.

3. Somatic symptoms: Operationally defined as the average score obtained on the Somatic Symptom Scale (SSS); based on a self-report scale with 20 items, wherein higher average scores indicate more severe somatic symptoms.

4. Neuroendocrine Levels: Operationally defined as the changes in serum/plasma levels of cortisol (COR), adrenocorticotropic hormone (ACTH), triiodothyronine (T3), thyroxine (T4), and thyroid-stimulating hormone (TSH) detected through blood testing; the levels of these markers indicate changes in neuroendocrine levels.

5. Anxiety disorder: A common psychological disorder characterized by persistent or excessive anxiety and worry that exceeds normal stress reactions. Features of anxiety disorders include persistent and uncontrollable worries and feelings of tension as well as anxiety-related physical symptoms, such as palpitations, difficulty breathing, muscle tension, and insomnia (Vahia, 2013).

1.8 Chapter summary

This chapter introduced important aspects related to the topic understudy and explained the significance of this study. This chapter specifically described the problem statement; outlined the research questions, research objectives, and hypotheses; presented the definitions of terms; and described the overall structure of this thesis. Chapter 2 presents a review of existing literature that is relevant to this study.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

This chapter presents background knowledge on somatic symptoms and neuroendocrine levels of anxiety disorders, CBT, and hypnotherapy as well as a comprehensive literature review on the importance of CH to provide a theoretical foundation for this study.

2.2 Characteristics of somatic symptoms in patients with anxiety disorders

Anxiety is an emotional state, and similar to other emotional states, it can be experienced in varying degrees of intensity, frequency, and duration. At the lower end of the scale, anxiety is adaptive and necessary for everyday life. However, when anxiety is over-expressed, in terms of magnitude, duration, and frequency, it can become overwhelming and destructive, evolving into different symptoms or even becoming pathological anxiety (Mallorquí–Bagué et al., 2016). The current uncontrolled and accelerating pace of life, increasing competition, and pronounced levels of personal emotional imbalance have led to a yearly increase in the prevalence of anxiety disorders (Sijie, 2019). According to a recent national survey study, anxiety disorders have the highest prevalence of all mental disorders at 4.98% (Huang et al., 2019). A cross-sectional survey of the prevalence of anxiety disorders in China conducted by Chinese scholar Huang Yuan at the beginning of the 2020 New Crown outbreak reported that the prevalence of anxiety disorders reached as high as 33.02%, and that of anxiety with somatization symptoms was 19.38% (Huang et al., 2020). The Bareeqa's survey in 2021 showed that among mood

disorders in China during COVID-19, the prevalence of anxiety disorders increased to 21.8%, and about 48.1% of people felt stressed due to COVID-19 (Bareeqa et al., 2021).

The prevalence of anxiety in China is higher than in other countries, particularly India and Singapore (Chew et al., 2020). According to Parker et al. (2001), when faced with anxiety and stress, Chinese people tend to deny their emotions and often manifest them physically. (Geng , 2013) reported that nearly half of Chinese patients with anxiety disorders often visit hospital outpatient clinics with somatic symptoms as the main manifestation, a phenomenon known as "Chinese somatization," which may be related to culture, customs, and other backgrounds. Chinese people are used to focus on somatic symptoms but less on psychological feelings (Ganlu, 2019).

Huang et al. (2020) found a significant correlation between somatic symptoms and the severity of anxiety symptoms in patients with anxiety disorders. People with anxiety disorders usually express their emotional and mental states through somatic symptoms. High levels of somatic symptoms often predict high levels of anxiety (Groen et al., 2021; Cai et al., 2017). In a study that analyzed the relationship between somatization symptoms and anxiety symptoms in patients with chronic pain, approximately half of the patients had varying degrees of anxiety; this finding indicates a significant correlation between somatization symptoms and anxiety disorders, and that the two can influence each other (Liao et al., 2019). Another study analyzed the degree of association between 200 patients with anxiety and somatization symptoms by using structural equation modeling; the results showed that somatization symptoms may aggravate anxiety symptoms (Bekhuis et al.,

2016). The study also suggests that if anxious and depressed patients are accompanied by more than two somatization symptoms at the same time, then their anxiety and depression states are relatively more difficult to improve and they often have residual symptoms.

A study investigated the causes of somatic symptoms in anxiety disorders and found that patients with anxiety disorders rated themselves higher than the control group in terms of somatic sensation, anxiety level, and self-sensitivity, suggesting that these patients have a high level of concern for their bodies. However, this high level of concern may not be related to the degree of physical change, meaning that patients may be accurate in their estimation of the direction of physical change, but not in their estimation of the degree of change. Researchers have explained that recurring somatic experiences create "memory imprints" in the brain that induce sensory experiences in the body, while actual physiological changes are minimal (Hoehn–Saric et al., 2004). In the theory of emotion proposed by James (Izard, 1990) , he suggests that physical changes are the origin of emotional changes; this hypothesis could explain the fact that people with anxiety disorders can be overly worried about somatic symptoms, which trigger anxiety, which in turn amplifies the feelings of somatic symptoms. Misattribution of somatic symptoms is one of the key factors in the development of anxiety disorders. Actual physical conditions, cognitive expectations, and interpretations of physical symptoms may exacerbate somatic symptoms in people with anxiety disorders (Mallorquí–Bagué et al., 2016). Other researchers have suggested that somatic symptoms are associated with the severity of the course of anxiety disorders. Longer duration of the anxiety disorder indicates higher probability that the patient will experience persistent somatic symptoms.

Therefore, considering somatic symptoms when treating patients with anxiety disorders may help improve their prognosis (Bekhuis et al., 2015).

Few studies have characterized the somatic symptoms of people with anxiety disorders and covered a narrow range of topics and a relatively homogeneous population. However, the most consistent finding for somatic symptoms is an increase in muscle tension (Chang et al., 2019) . A survey showed that more than 30% of patients with anxiety in psychiatric–psychological outpatient clinics in Chinese general hospitals had concomitant somatic symptoms with a complex and varied clinical presentation involving multiple systems and organs throughout the body and often blurred (Su et al., 2014). Huang et al. (2004) reported that the subjective somatic discomfort of patients with anxiety is mainly characterized by autonomic symptoms (e.g., palpitations, sweating, and trembling).

Gupta's research showed that people with anxiety disorders often experience symptoms, such as dyspnea, shortness of breath, and chest tightness (Gupta & Simpson, 2015). Respiratory functioning in people with anxiety disorders is closely related to cognitive and emotional states. Patients with anxiety and anxiety disorders also experience symptoms, such as palpitations, tachycardia, and elevated blood pressure during anxious states. The dysregulation of the autonomic nervous system in patients with anxiety disorders is associated with cardiovascular symptoms. Sympathetic activity is increased in anxiety states, leading to the development of circulatory symptoms, such as increased heart rate and elevated blood pressure. Respiratory activity increases with increasing respiratory rate and depth, leading to the development of symptoms, such as dyspnea (Benarroch, 1993). Symptoms, such as indigestion, abdominal pain, and nausea, also occur. Yang (2015) found that stress

hormones and neurotransmitter changes in the body during anxiety states led to increased gastrointestinal motility and increased secretion of digestive juices, which cause digestive symptoms. Patients with anxiety disorders often experience symptoms of endocrine disruption, such as excessive sweating, hand tremors, and fatigue. The release of stress hormones, such as COR and epinephrine increases, during anxiety, leading to the disruption of the neuroendocrine system, which in turn causes somatic symptoms (Hinds & Sanchez, 2022).

2.3 Characteristics of neuroendocrine function in patients with anxiety disorders

A close correlation exists among emotions, nervous system, and endocrine system of humans. People with anxiety disorders usually exhibit symptoms, such as fidgeting, nervousness, and autonomic disorders (Liu, 2018). The experience of anxious emotions is the main feature of anxiety disorders, and psychological emotions can considerably affect the body's neuroendocrine system. Therefore, when treating anxiety disorders, the relationship between anxiety disorders and neuroendocrine dysfunction should be understood to improve the effectiveness of treatment. With the progress of neuroendocrine research on anxiety disorders, the hypothalamus–pituitary–adrenal (HPA) axis and the hypothalamic–pituitary–thyroid (HPT) axis are closely related to mental activity and behavior. Chronic stress can significantly activate the HPA axis, and that negative emotions, such as worry and anxiety, are strongly associated with HPA axis dysfunction and may lead to abnormal serum COR levels (Guilliams & Edwards, 2010).

Some authors have put forward the idea that anxiety disorders are stressor-related disorders that manifest in patients' core endocrine response to stress, thereby activating the HPA axis, which leads to an increase in COR levels (Axelrod & Reisine, 1984). Stress, whether physical or emotional (Benjamins et al., 1992) or acute or chronic (Bloom & Kupfer, 1995), can lead to activation of the HPA axis. The hypothalamic release of the hormone corticotropin-releasing factor (CRF), a hypothalamic neuropeptide that activates the pituitary–adrenal system, has been implicated in the pathophysiology of anxiety disorders (Arborelius et al., 1999; Benjamins et al., 1992). Increased release of CRF may be one of the causes of many anxiety symptoms (Butler & Nemeroff, 1990). ACTH is a hormone released by the pituitary gland, and COR is the hormone released by the adrenal cortex. COR has a negative feedback regulation of CRH and ACTH, and its level fluctuates with the circadian physiological rhythm of the HPA axis; the highest value occurs when waking up in the morning, and the morning COR level can be a good reflection of the functional state of the adrenal cortex (Honglei, 2011).

Steimer (2002) found that HPA axis hormones, such as COR and ACTH, are usually increased during anxiety and fear. Hilbert et al. (2014a) also indicated that COR is associated with negative emotions, especially potential COR as an indicator of altered HPA activity in Generalized Anxiety Disorder (GAD). The relationship between anxiety and COR levels appears to yield inconsistent findings across various studies. Some investigations report a positive correlation between anxiety levels, as measured by the SAS Anxiety Measurement Scale and COR output (Dong et al., n.d.). Other studies suggest that individuals with anxiety disorders may exhibit heightened HPA function and elevated plasma COR levels during stress (Dailin et al.,

2017a; Yin Honglei, 2016). However, conflicting results emerge, with some studies indicating lack of significant change or even lower COR levels compared with normal individuals (Bin et al., 2019). Discrepancies exist regarding the timing of COR elevation, with some studies observing higher levels in the afternoon (Hood et al., 2011) and others noting no significant changes in the morning (Tafet et al., 2001).

HPT research by Fischer & Ehlert (2018) found the relationship of comorbidity to thyroid disorders and anxiety, and anxiety-related symptoms are very common in hyperthyroid disorders. Shen et al. (2012) found that in the HPT axis, the hormone released by the hypothalamus is thyrotropin-releasing hormone (TRH), the hormone released by the pituitary gland is thyrotropin (TSH), and the hormone released by the thyroid gland of the peripheral organs is thyroxine, which includes T3 and T4. The levels of thyroid hormones can well reflect the functional status of the HPT axis. The endocrine system transmits signals to the central nervous system and regulates the physiological functions and emotional state of the body. In patients with anxiety disorders, the endocrine system is often dysfunctional. Several studies have found that the pituitary–adrenocortical axis (HPA axis) is overactive in people with anxiety disorders, and hypnotherapy can improve endocrine levels in people with anxiety disorders by modulating the activity of the HPA axis. The HPA axis is a major regulator of the stress response, and hypnotherapy can alleviate the stress response in people with anxiety disorders by decreasing the level of activity of the HPA axis (Alladin, 2012). A close connection exists between anxiety disorders and thyroid function. The thyroid function and mental activity have a close relationship, that is, as the thyroid hormone disorders will affect the patient's brain tissue, leading to abnormal nerve and mental state (Lishu & Jian, 2016).

In China, limited information is available on the involvement of HPT axis on anxiety disorders and their patients. Condren (2002) reported the correlation between temperament traits and personality factors with neurotransmitters and neuroendocrine function in patients with anxiety disorders. Yin Honglei (2011) found that TSH levels were significantly elevated in the blood of patients with anxiety disorders compared with normal controls, suggesting that the HPT axis is activated in patients with anxiety disorders. In Europe and the United States, few studies have shown a close link between anxiety disorders and thyroid function (Hilbert et al., 2014a). Simon (2002) found that patients with anxiety disorders have an increased risk of lifetime prevalence of thyroid dysfunction due to abnormal functioning of the HPT axis. Mauro Giovanni et al. (2004) suggested that thyroid antibodies are associated with anxiety disorders. In addition, some genes may increase susceptibility to certain disorders, including panic disorder, mitral valve prolapse, and thyroid disorders. This finding suggests that panic disorder and thyroid disorders may share common susceptibility genes (Hamilton et al., 2003).

2.4 CBT in patients with anxiety disorders

In a previous epidemiologic survey of anxiety disorders, we learned that anxiety disorders are currently the most prevalent mental disorders in China. According to the Diagnostic and Statistical Manual of Mental Disorders ICD-10 (World Health Organization ,1992), anxiety disorders are categorized into different types (e.g., panic disorder, generalized anxiety disorder, social phobia, etc.), which share similar characteristics of fear and excessive anxiety and lead to behavioral disorders. These disorders often have a significant effect on people's daily lives (Andrews et al., 2001; Barrera & Norton, 2009; Olatunji et al., 2007).

CBT is considered the gold standard in the psychotherapy of anxiety disorders (Olatunji et al., 2010); it combines behavioral and cognitive interventions guided by the principles of applied science. Behavioral interventions aim to improve maladaptive behavior and increase adaptive behaviors by changing the antecedents and consequences of the patient's behavior as well as learning new behavior and practicing them. Cognitive interventions aim to change patients' maladaptive cognitions and self-unreasonable beliefs. The core feature of CBT is problem solving strategies based on learning and cognitive theories (Arch & Craske, 2009; Craske, 2010; Norton & Price, 2007). The use of CBT is effective in treating a variety of anxiety disorders, including panic disorder, generalized anxiety disorder, social anxiety disorder, and so on.

In 2020 during COVID-19, Li et al. (2020) conducted a randomized controlled trial of CBT for patients affected by anxiety, depression, and stress; the results showed that anxiety, depression, and stress scores of patients in the intervention group decreased substantially after treatment, and the length of hospital stay in the intervention group was shorter than that in the control group. Hofmann et al. (2014) conducted a meta-analysis of the effects of CBT for anxiety disorders on quality of life; the results showed that CBT was effective in improving quality of life, especially in the physical and psychological domains. Treatments delivered in web-based online and video modalities were not as effective as face-to-face treatments in improving quality of life. Perihan et al. (2020) confirmed that CBT provided moderate relief of anxiety symptoms in children under Autism Spectrum Disorder (ASD). It has a good therapeutic effect. Donegan & Dugas (2012) compared the course of symptom change in patients with GAD who received either CBT or

Relaxation Therapy (RT) and found that both therapies were effective in treating patients with GAD; however, the effect of CBT on somatic anxiety change was more significant. Moonen et al. (2021) showed that in Parkinson's comorbid anxiety disorders, the application of CBT will reduce situational and social anxiety and avoidance behavior among patients.

CBT is a practical and structured form of psychotherapy. It can be delivered by a therapist on a one-to-one basis or in a group setting with multiple patients suffering from the same illness and with the same symptoms. The group model of CBT has several advantages: first, the therapist can work with a larger number of people in a session rather than treating them individually. Second, many patients find it helpful to meet others with similar difficulties; they can help each other and share experiences. For individuals with social fears, the group format can provide opportunities for socialization. Third, patients can provide different perspectives and feedback because they come from different upbringings and backgrounds. Fourth, it can reduce the patient's sense of isolation and loneliness. In group therapy, patients can develop connections and friendships with other group members and share each other's experiences and feelings. This sense of connection and belonging is important for the patient's mental health and emotional regulation and contributes to increased self-esteem and self-acceptance (Norton, 2012).

Current research has developed a number of cognitive behavioral group therapies (CBGT) for specific anxiety disorders. For example, Neufeld et al. (2020) conducted a randomized clinical trial of group and individual cognitive behavioral therapies for social anxiety disorders; the results showed that both treatments were equally effective in reducing symptoms of different comorbid disorders in patients

with SAD. Davis (2012) and Neufeld et al. (2020) conducted a literature review of group psychotherapy for social fears and found that CBGT received the most support for its effectiveness in treating social phobias. Raffin et al. (2009) evaluated the predictors of response to CBGT in the treatment of OCD; they reported that CBGT was more effective for women than for men, and that alleviation of anxiety symptoms could significantly improve obsessive–compulsive symptoms in patients with OCD if they have comorbid symptoms, such as anxiety. Bilet et al. (2020) studied CBGT treatment for panic disorder with a follow-up of 12 to 31 years; they found the effects on the mental health and quality of life at the end of the treatment, and such effects remained stable thereafter. At long-term follow-up, 98% of patients had a 50% reduction in their total score on a fear avoidance-related scale, and 93% were satisfied with the results.

Koffel et al. (2015a) conducted a meta-analysis of CBGT for insomnia and found Cognitive Behavior Therapy for Insomnia (CBT-I) could be an effective treatment for insomnia, particularly in terms of sleep latency, sleep efficiency, and awakening after sleep onset; they also stated that the treatment improved the total sleep time, sleep quality, and symptoms of depression and pain. In a meta-analysis on the effects of CBGT on depression, CBGT had a sustained effect on depressed patients for up to 6 months. The take-home assignments during CBGT improved the effect, indicating that assigning appropriate homework can help patients apply CBT in their daily lives (Feng et al., 2012). Hunot's study summarized the efficacy of CBT in the treatment of subtypes of anxiety disorders, such as generalized anxiety disorder, social anxiety disorder, and panic disorder, through a systematic review and meta-analysis of several clinical trials (Hunot et al., 2007). CBT significantly

reduced anxiety symptoms, with more consistent results for generalized and social anxiety disorders. No significant difference was found in the treatment of panic disorder when compared with medication.

Kosecki & Firth (2020) explored the comparison of CBT with hypnotherapy in the treatment of anxiety disorders. CBT and hypnotherapy were effective in reducing anxiety symptoms, but CBT had a more lasting effect at long-term follow-up. Several studies (Butler et al., 2006; Hofmann & Smits, 2008) showed that CBT is an effective treatment for anxiety disorders because it reduces anxiety symptoms by helping patients to change their perceptions of and ways of coping with anxiety triggers and that its effects are stable across subtypes of anxiety disorders.

CBT has evolved to the present day, and its therapeutic effects on anxiety disorders have been widely validated; however, problems and questions have persisted, such as the fact that a significant portion of visitors drop out of treatment halfway through the course of treatment, do not show significant improvement in their symptoms, or experience relapses in subsequent treatments; as such, integration with other therapies is imperative (Wolitzky-Taylor et al., 2012)

2.5 Hypnotherapy in patients with anxiety disorders

Hypnosis is an ancient Western therapeutic concept (Ellenberger, 1970) that has been used for over 200 years as an adjunct tool for treating traumatic experiences, pain, and anxiety. Its initial application involves hypoalgesia to help patients undergo traumatic surgeries before the onset of anesthesia (Patterson, 2003). Hypnosis is a state of highly focused attention and consists of three parts: absorption, dissociation, and suggestion. Suggestion does not mean that the hypnotized individual is unable to

control their thoughts and actions, but rather that they are inclined to accept hypnotic suggestions. In hypnosis, people are more focused on "what" rather than “why,” making them more susceptible to compliance. This practice actually helps patients break free from old maladaptive ways of coping with anxiety and other issues (Tellegen, 1981; Tellegen & Atkinson, 1974).

Anxiety disorder is a typical psychosomatic illness. The interaction between the physical and psychological symptoms of anxiety disorder leads to a vicious cycle of mental and physical distress in patients, thereby creating a "snowball" effect. When patients notice their heart rate increasing, are sweating, or are having muscle tension, they may become more anxious and interpret these bodily signals as indications of being in a tense state. This phenomenon then triggers physical reactions, so techniques, such as hypnosis, which involve enhancing control of thoughts over the body, are particularly important in treatment (Spiegel, 2013). Hypnosis not only alleviates anxiety in patients with anxiety disorder but also relaxes their tense muscles. The dissociation aspect of hypnosis also helps patients with anxiety disorder separate their anxious physical symptoms from their psychological ones, allowing them to focus on anxiety issues and dissociate from uncomfortable physical symptoms. Evidence indicates that hypnosis is as effective as 1 mg of alprazolam in reducing anxiety among university students (Garvin et al., 2001; Nishith et al., 1999; Spiegel, 2007). Hypnosis therapy has been widely used in patients with anxiety disorders. As early as over 20 years ago, scholars (Galovski & Blanchard, 2002; Whorwell et al., 1984) reported successful treatment of patients suffering from irritable bowel syndrome (IBS) and GAD who had failed various

psychological treatments but achieved significant improvement in IBS and GAD symptoms after hypnosis therapy.

Daitch (2014) found that hypnosis can increase cognitive flexibility and bypass subconscious self-defense and conscious resistance when conducting hypnotherapy for anxiety-related discordant relationships. Therefore, it affects the attitudes and changes the understanding of patients, producing new reactions and communication patterns that are beneficial to anxious and non-anxious partners. In addition, Hammond (2010a) found that self-hypnosis is a rapid, cost-effective, non-addictive, and safe treatment for anxiety-related disorders. Siregar et al. (2022) reported the use of hypnosis to relieve antenatal anxiety in pregnant women who developed a standardized self-hypnosis manual; the treatment can effectively alleviate anxiety in pregnant women and help them remain calm and relaxed during childbirth. Prabowo (2021) developed a theoretical model of self-hypnosis in a study on anxiety and pain in patients with general anesthesia; the results showed that applying the Self-Hypnosis Model (SHM) can reduce anxiety and pain in patients after general anesthesia. With the development of technology and the popularity of the Internet, the use of audio for self-hypnosis has become an emerging hypnotherapy method. Self-hypnosis was used as a part of cognitive behavior interventions in addition to hypnosis interventions for patients with anxiety due to obesity; researchers found that the effect was greater when self-hypnosis was used compared with not using self-hypnosis (Milling et al., 2018).

In a meta-analysis of the effectiveness of hypnosis for dental anxiety and phobia, Wolf et al. (2022) found that many studies used recorded hypnosis to help patients alleviate preoperative anxiety; about 70% of the studies indicated that

recorded hypnosis can effectively relieve dental anxiety. Flik et al. (2019) found that group hypnosis therapy for patients with IBS is not inferior to individual hypnosis therapy, and the former allows more patients to receive treatment at the same price, thereby saving time and economic costs. Fisch & Silvia (2020) also stated that group hypnosis effectively reduces patients' stress and improves their coping mechanisms for stress. Elkins et al. (2015) conducted a randomized controlled trial to compare the effects of hypnosis therapy and conventional therapy on patients with anxiety disorders. The hypnosis therapy group demonstrated significant improvements in anxiety symptoms, depressive mood, and quality of life, outperforming the conventional therapy group. Alladin (2012) conducted a long-term follow-up observation on patients with anxiety disorder treated with hypnosis therapy and found that their anxiety symptoms continued to decrease steadily. Moreover, noticeable improvements were found in their social functioning, self-confidence, and self-esteem. Kirsch (1996) and Montgomery et al. (2007) indicated that hypnosis therapy has some effectiveness in treating anxiety disorders. Hypnosis therapy can adjust patients' cognition, emotions, and behavior by altering their conscious state, thereby alleviating anxiety symptoms. It can also help patients relax physically and mentally, thereby improving their sleep quality and overall quality of life.

No therapy can be perfect, and all therapies have their limitations (Wu Bo, 2019). Although hypnosis therapy was initially used as an independent psychological treatment method in clinical therapy and many studies have shown its effectiveness and fast results, it lacks the core theoretical basis of psychological treatment and behavior change. Additionally, it encompasses numerous techniques, hence the need for integration with other psychological therapies (Shu, 2013).

2.6 CBT combined hypnotherapy in patients with anxiety disorders

CBT has a relatively complete theoretical foundation and related therapeutic techniques. However, since its establishment, CBT has particularly emphasized the use of logic and reasoning to solve emotional problems. It emphasizes rationality, logic, and focus on the conscious domain of the subject, rather than directly addressing the unconscious domain. Therefore, CBT cannot directly restructure negative beliefs in the subconscious but mainly achieves cognitive restructuring through reasoning and Socratic dialogue (Stricker & Gold, 2013).

Clinical practitioners have started to integrate hypnotherapy and cognitive theory (Alladin & Alibhai, 2007). By combining hypnotherapy with CBT, hypnotherapy has gained a solid theoretical foundation and has changed the paradigm of CBT, which previously only focused on consciousness. It has increased attention to the unconscious domain, allowing it to focus on the conscious and unconscious domains of the patient. This integration enables cognitive restructuring to be directly applied to patients at the conscious and unconscious levels.

Cognitive behavior hypnotherapy (CBH) is rooted in CBT and incorporates hypnosis, with a focus on individual thinking and behavioral patterns in specific situations as well as overcoming emotional and behavioral problems. The integration of hypnosis techniques with CBT was proposed in 1994 to enhance treatment effects and is referred to as CBH. This strategy provides additional treatment by promoting the reduction of symptoms (Alladin, 1994). Combining hypnosis techniques with CBT has several advantages. First, patients are more motivated to engage in treatment while in a hypnotic state, reducing resistance during therapy. Improving patient motivation can be beneficial to some extent. Second, hypnosis can work with

the patient's subconscious, enhancing positive cognition during treatment and then implementing behavioral therapy in a conscious state. Last, the use of hypnotic induction techniques can help relax the patient's muscles, focus their attention, and promote faster relaxation and reduced anxiety (Brooker, 2020). Some researchers have already used CBT combined with hypnosis to enhance treatment effects, and some studies have demonstrated the effectiveness of this integration.

Jensen & Mark (2020) found that the use of cognitive hypnosis therapy can effectively reduce the intensity of pain, resulting in a 39% decrease in pain perception. Asadi & Aghaei (2021) conducted a survey comparing CBT, hypnosis, and cognitive hypnosis therapy on female somatic symptoms and sexual satisfaction. They found that cognitive hypnosis therapy can alleviate somatic symptoms and improve female sexual satisfaction. Baharvand et al. (2022) also found that cognitive hypnosis therapy is more effective than CBT and that eye movement desensitization and reprocessing (EMDR) can reduce anxiety levels and improve autobiographical memory, making it more positive. Ramondo et al. (2021) in the meta-analysis of cognitive hypnosis showed a large number of literature indicating that CBH is more effective than using CBT alone. In a tracking study by Bryant et al. (2005), researchers randomly divided patients with acute stress disorder into three groups and conducted CBT, Group Cognitive behavior Hypnotherapy (GCBH), and supportive counseling interventions. The results showed that the GCBH significantly reduced re-experiencing symptoms after treatment compared to CBT and maintained significant effects after 6 months.

Cognitive hypnosis therapy is also widely used in patients with anxiety disorders. Chapman & Robin (2005) used cognitive hypnosis therapy to alleviate